

**Table S6**

Enriched KEGG pathway terms by genes over-expressed in each ESCC subtype.

Enriched KEGG pathway terms by genes over-expressed in Subtype I ESCC												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
KEGC	hsa04514:Cell adhesion mole	64	0.261534	1.71E-18	CLDN8, CLDN7, CADM1	802	132	5085	3.074133	0.000000	0.000000	0.000000
KEGC	hsa04672:Intestinal immune r	29	0.118508	3.06E-11	HLA-DQB1, HLA-DRB1,	802	49	5085	3.752481	0.000000	0.000000	0.000000
KEGC	hsa05330:Allograft rejection	22	0.089902	5.73E-09	HLA-DQB1, PRF1, HLA-I	802	36	5085	3.874688	0.000001	0.000000	0.000007
KEGC	hsa04940:Type I diabetes mel	24	0.098075	5.74E-09	HLA-DQB1, PRF1, ICA1,	802	42	5085	3.623085	0.000001	0.000000	0.000007
KEGC	hsa05332:Graft-versus-host d	22	0.089902	3.99E-08	HLA-DQB1, PRF1, HLA-I	802	39	5085	3.576635	0.000007	0.000001	0.000049
KEGC	hsa05340:Primary immunode	20	0.081729	1.51E-07	CIITA, PTPRC, CD3D, CI	802	35	5085	3.623085	0.000027	0.000005	0.000186
KEGC	hsa05310:Asthma	18	0.073556	1.53E-07	HLA-DQB1, HLA-DRB1,	802	29	5085	3.935420	0.000028	0.000004	0.000189
KEGC	hsa04060:Cytokine-cytokine i	72	0.294226	1.00E-06	IL21R, TNFSF15, IL13, F/	802	262	5085	1.742400	0.000181	0.000023	0.001236
KEGC	hsa04062:Chemokine signalir	55	0.224756	2.69E-06	ADCY1, PREX1, ADCY5,	802	187	5085	1.864823	0.000483	0.000054	0.003309
KEGC	hsa05320:Autoimmune thyro	22	0.089902	1.10E-05	HLA-DQB1, PRF1, HLA-I	802	51	5085	2.735074	0.001978	0.000198	0.013546
KEGC	hsa04640:Hematopoietic cell	30	0.122594	2.62E-05	HLA-DRB1, CD8A, CD8E	802	86	5085	2.211767	0.004700	0.000428	0.032233
KEGC	hsa04660:T cell receptor sign	35	0.143026	2.83E-05	CD8A, CD8B, CD247, PD	802	108	5085	2.054759	0.005074	0.000424	0.034803
KEGC	hsa04662:B cell receptor sign	27	0.110335	3.97E-05	CD72, BTK, RASGRP3, C	802	75	5085	2.282544	0.007113	0.000549	0.048834
KEGC	hsa00982:Drug metabolism	23	0.093989	1.04E-04	GSTA2, CYP3A7, CYP2C	802	62	5085	2.352084	0.018548	0.001336	0.128033
KEGC	hsa04612:Antigen processing	27	0.110335	2.67E-04	HLA-DQB1, KLRC4, KLF	802	83	5085	2.062539	0.046920	0.003199	0.328314
KEGC	hsa05416:Viral myocarditis	23	0.093989	9.17E-04	HLA-DQB1, ITGAL, PRF	802	71	5085	2.053932	0.152155	0.010263	1.123142
KEGC	hsa04610:Complement and cc	22	0.089902	0.001534806	C3AR1, C7, A2M, CR1, F/	802	69	5085	2.021576	0.241549	0.016132	1.874162
KEGC	hsa05322:Systemic lupus eryt	28	0.114421	0.002197819	HLA-DQB1, C7, HLA-DR	802	99	5085	1.793244	0.327022	0.021762	2.673744
KEGC	hsa04020:Calcium signaling f	43	0.175718	0.002831862	SLC8A3, GNA14, CCKAF	802	176	5085	1.549075	0.399780	0.026509	3.432786
KEGC	hsa00980:Metabolism of xenc	19	0.077643	0.00386801	GSTA2, CYP1B1, CYP3A	802	60	5085	2.007793	0.502217	0.034278	4.661505
KEGC	hsa00830:Retinol metabolism	17	0.06947	0.007175994	CYP3A7, CYP2C19, CYP.	802	54	5085	1.996052	0.726468	0.059864	8.488804
KEGC	hsa04650:Natural killer cell r	33	0.134854	0.007558569	ITGAL, PRF1, KLRC3, CI	802	133	5085	1.573182	0.744801	0.060190	8.922208
KEGC	hsa04960:Aldosterone-regula	14	0.057211	0.008033189	PIK3CG, IRS4, IRS2, ATP	802	41	5085	2.165014	0.765855	0.061171	9.457266
KEGC	hsa00590:Arachidonic acid m	17	0.06947	0.010430382	CYP2U1, TBXAS1, CYP2	802	56	5085	1.924764	0.848524	0.075626	12.115856
KEGC	hsa05218:Melanoma	20	0.081729	0.011645805	PIK3CG, FGFR1, FGF7, F	802	71	5085	1.786028	0.878586	0.080883	13.436231
KEGC	hsa00260:Glycine, serine and	11	0.044951	0.016891076	CHDH, GATM, SDS, MA	802	31	5085	2.249819	0.953410	0.111248	18.928016
KEGC	hsa04670:Leukocyte transend	28	0.114421	0.025439025	CLDN8, CLDN7, ITGAL,	802	118	5085	1.504501	0.990326	0.157842	27.195999
KEGC	hsa05414:Dilated cardiomyop	23	0.093989	0.025872694	SLC8A3, CACNA2D1, AI	802	92	5085	1.585100	0.991070	0.155081	27.594044
KEGC	hsa00380:Tryptophan metabo	12	0.049038	0.040457967	DDC, CYP1B1, MAOA, A	802	40	5085	1.902120	0.999409	0.226121	39.872428
KEGC	hsa04360:Axon guidance	29	0.118508	0.043510585	DCC, PLXNC1, LRRRC4,	802	129	5085	1.425361	0.999667	0.234261	42.186628
KEGC	hsa04664:Fc epsilon RI signa	19	0.077643	0.05628816	PIK3CG, LYN, IL13, MAI	802	78	5085	1.544456	0.999970	0.285658	51.012556
KEGC	hsa00350:Tyrosine metabolis	12	0.049038	0.074697855	DDC, TYRPI, MAOA, M/	802	44	5085	1.729200	0.999999	0.353833	61.567518
KEGC	hsa00120:Primary bile acid bi	6	0.024519	0.093356992	CYP7B1, BAAT, CYP27A	802	16	5085	2.377650	1.000000	0.414085	70.096464

  

Enriched KEGG pathway terms by genes over-expressed in Subtype II ESCC												
Category	Term	Count	%	PValue	Genes	List Total	Pop Hits	Pop Total	Fold Enrichment	Bonferroni	Benjamini	FDR
KEGC	hsa04510:Focal adhesion	57	0.205265	2.54E-06	HRAS, PGF, BCAR1, VTN	781	201	5085	1.846370	0.000439	0.000439	0.003108
KEGC	hsa05130:Pathogenic Escheri	24	0.086427	3.98E-06	ACTB, YWHAZ, TUBB2/	781	57	5085	2.741425	0.000688	0.000344	0.004871
KEGC	hsa04810:Regulation of actin	57	0.205265	2.31E-05	FGF5, HRAS, BCAR1, GN	781	215	5085	1.726141	0.003995	0.001333	0.028308
KEGC	hsa04512:ECM-receptor inter	26	0.093663	5.47E-04	TNC, ITGB4, VTN, SDC4	781	84	5085	2.015273	0.090354	0.023397	0.667548
KEGC	hsa05200:Pathways in cancer	70	0.25208	0.002702581	FGF5, PPARD, HRAS, PG	781	328	5085	1.389518	0.373859	0.089386	3.257091
KEGC	hsa04621:NOD-like receptor	19	0.068422	0.004257835	CXCL1, HSP90AA2, HSP	781	62	5085	1.995271	0.522016	0.115763	5.086998
KEGC	hsa04012:ErbB signaling path	24	0.086427	0.004921243	EGFR, HRAS, NRG4, MA	781	87	5085	1.796106	0.574069	0.114785	5.857846
KEGC	hsa04540:Gap junction	24	0.086427	0.006634817	EGFR, HRAS, GNAI3, AI	781	89	5085	1.755744	0.683885	0.134074	7.822413
KEGC	hsa05219:Bladder cancer	14	0.050416	0.008007206	EGFR, HRAS, IL8, PGF, C	781	42	5085	2.170294	0.751129	0.143187	9.368593
KEGC	hsa00010:Glycolysis / Glucon	17	0.061219	0.016062843	ALDOA, LDHA, ALDOC,	781	60	5085	1.844750	0.939277	0.244324	17.974356
KEGC	hsa04010:MAPK signaling pa	55	0.198063	0.016614038	FGF5, HRAS, ZAK, GNA	781	267	5085	1.341193	0.944887	0.231633	18.534830
KEGC	hsa04530:Tight junction	31	0.111635	0.018221523	PRKCZ, HRAS, GNAI3, Z	781	134	5085	1.506249	0.958472	0.232883	20.149355
KEGC	hsa04520:Adherens junction	20	0.072023	0.021027425	EGFR, ACTB, BAIAP2, T	781	77	5085	1.691139	0.974689	0.246337	22.897318
KEGC	hsa04912:GnRH signaling pa	24	0.086427	0.021354232	EGFR, PLD2, HRAS, PLD	781	98	5085	1.594502	0.976110	0.234124	23.211666
KEGC	hsa05211:Renal cell carcinom	18	0.06482	0.032487097	HRAS, PGF, MET, EGLN:	781	70	5085	1.674227	0.996699	0.316758	33.242778
KEGC	hsa04150:mTOR signaling pa	14	0.050416	0.046362815	PGF, RPS6KB2, RPTOR, I	781	52	5085	1.752930	0.999729	0.401477	44.058317
KEGC	hsa00564:Glycerophospholipi	17	0.061219	0.048543412	PLD2, PLD1, CRLS1, NA	781	68	5085	1.627721	0.999817	0.397335	45.603539
KEGC	hsa04722:Neurotrophin signa	27	0.097231	0.055241771	HRAS, YWHAZ, NFKBIA	781	124	5085	1.417692	0.999946	0.420832	50.108398
KEGC	hsa05216:Thyroid cancer	9	0.03241	0.064832095	LOC407835, MAPK1, NR.	781	29	5085	2.020619	0.999991	0.456822	55.963858
KEGC	hsa04210:Apoptosis	20	0.072023	0.065617599	RELA, NFKBIA, ENDOD	781	87	5085	1.496755	0.999992	0.444047	56.414315
KEGC	hsa04060:Cytokine-cytokine i	50	0.180057	0.074272974	OSMR, IL28RA, TGFB1, I	781	262	5085	1.242535	0.999998	0.470479	61.105327
KEGC	hsa04360:Axon guidance	27	0.097231	0.082098981	ABLIM2, HRAS, PLXNA:	781	129	5085	1.362743	1.000000	0.490153	64.942946
KEGC	hsa04666:Fc gamma R-media	21	0.075624	0.082236067	PLD2, PLD1, VAV3, LIM	781	95	5085	1.439248	1.000000	0.475589	65.006956
KEGC	hsa04670:Leukocyte transend	25	0.090028	0.084819892	ACTB, GNAI3, VAV3, GN	781	118	5085	1.379424	1.000000	0.472131	66.193519
KEGC	hsa05120:Epithelial cell signa	16	0.057618	0.088194711	EGFR, CXCL1, ADAMI0.	781	68	5085	1.531973	1.000000	0.472135	67.687693
KEGC	hsa03050:Proteasome	12	0.043214	0.094865352	PSMF1, PSMB7, PSMC6,	781	47	5085	1.662353	1.000000	0.484800	70.464194
KEGC	hsa05221:Acute myeloid leuk	14	0.050416	0.097262298	HRAS, PPARD, RELA, PI	781	58	5085	1.571593	1.000000	0.480883	71.407119